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22. A method as claimed in claim 16, wherein said RNase is onconase.--

REMARKS

Claims 1-19 are pending. Applicants affirm their election of Group I, claims 1-15 for initial consideration on the merits. Claim 20 has been added, as supported by the paragraph bridging pages 1 and 2. Claims 21-22 have been added based on page 8, lines 14 and 15. Claims 1-22 remain in the case.

Claims 16-19 are withdrawn from consideration. Claims 1-15 and 16-19 are related as product and process of use. If an applicant elects claims directed to a product, and the product is subsequently found allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product will be rejoined and examined by the examiner.[1] Once the product claims are found allowable in this case, claims 16-19, to a process of using a fusion protein that includes all the limitations of the product claims, should be rejoined and examined.[2]

Forwarded with this response is a Sequence Listing, to comply with 37 CFR §1.821 through §1.825. The specification has been amended accordingly.

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[1] Claim 16 has been amended to include all limitations of the product claims.

[2] *In re Ochiai*, 37 USPQ2d 1127 (Fed. Cir. 1995); *In re Brouwer*, 37 USPQ2d 1663 (Fed. Cir. 1996); "Training Materials for Treatment of Product and Process Claims in Light of *In re Brouwer* and *In re Ochiai*" (Office of Patent Policy Dissemination, Patent Academy).

Applicant notes that claims 2, 4 and 5 are objected to as dependent on a rejected base claim, but are otherwise allowable. In addition, claims 8-15 are subject only to a rejection under the first paragraph of §112, and thus are free of the prior art.

Claims 8-15 are rejected under the first paragraph of §112 as lacking enablement. The examiner finds that the specification enables a fusion protein comprising a bispecific antibody that has a first specificity for CD20 and a second specificity for a region of IL-15α, but contends that the specification does not enable a fusion protein comprising a bispecific antibody that has a first specificity for a cell marker specific to a malignant cell and a second specificity for a region of Il-15α. In this regard she argues that "there are no specific cell markers known that are specific to malignant cells," and that in order to practice the invention the artisan would have to know how to deliver the therapeutic agent so that it would not kill non-malignant cells and, in particular, so that it would not destroy the normal function of the immune system.

Cancer therapy using antibodies to antigens expressed on malignant cells, such as the LL2 anti-CD22 mAb, is a widely-accepted therapeutic approach. For example, the present specification references "a fairly large and growing body of experience in the use of monoclonal antibodies (mAbs) for the therapy of lymphoma," including the use of different B-cell restricted CD (clusters of differentiation). More particularly, preliminary studies using LL2 labeled with ^{131}I for both therapy and imaging of NHL have produced response rates of

30-90+%, with varying percentages of complete responses and differences in durability of response.

While it is true that antibodies such as LL2 also will bind to non-malignant cells, binding is much higher for malignant cells. This is so because the malignant cells express the cognate antigen much more highly than do non-malignant cells. By merely managing the dose, it often is possible to kill malignant cells without unduly damaging non-malignant cells. In cases where higher doses are necessary to kill the malignant cells, adjunct therapy with cytokines and/or autologous bone marrow or peripheral stem cell rescue can be used as part of an effective therapy. Accordingly, one of ordinary skill in the art is clearly able to practice the present invention. Reconsideration and withdrawal of the rejection of claims 8-15 under the first paragraph of §112 is respectfully requested.

Claims 1 and 6 stand rejected under §102(b) based on Verheul *et al.*, and claim 3 stands rejected under §103(a) based on Verheul *et al.* in view of Anderson *et al.* Claim 1 has been amended to incorporate the recitation of claim 2 that the toxin is an RNase, thereby obviating the rejections under both §102 and §103(a) that are based on Verheul.

Claims 1, 6 and 7 stand rejected under §102(b) based on Mallinckrodt Medical. The examiner urges that Mallinckrodt Medical, Inc. discloses conjugates with IL-2. However, Mallinckrodt Medical discloses conjugates with IL-8, and not with IL-2. The examiner also is incorrect in alleging that Mallinckrodt Medical "teach a conjugate

of a therapeutic radionuclide and a cell-specific cytokine." To the contrary, Mallinckrodt Medical is directed to "a labelled CXC chemokine [utilized] to ***image*** a target site in an animal's body" and does not suggest conjugates with a ***therapeutic*** radionuclide. In this regard, the document details the "several *a priori* advantages for clinical nuclear imaging" that are provided by IL-8. Thus claims 1, 6 and 7 are not anticipated or rendered obvious based on Mallinckrodt Medical.

In view of the amendments to the claims and the foregoing remarks, it is believed that all claims are in condition for allowance. Reconsideration of all rejections and a notice of allowance are respectfully requested. Should there be any questions regarding this application, Examiner Mertz is invited to contact the undersigned attorney at the phone number listed below.

Respectfully submitted,

Dec. 28, 1998
Date

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The Commissioner is hereby authorized to charge any fee required by the filing of this response to Deposit Account No. 19-0741.